subject application provides generous support and teachings that demonstrate the ability to generate a therapeutic immune response through use of the claimed methods. While Applicants maintain that the subject methods are useful for gene therapy purposes, Applicants have amended claims 1 and 27 to recite that an immune response is induced, which is clearly enabled by teachings of the subject application. As described in Example 12 of the specification, Applicants have shown that pretreatment with a disruptive agent (ethanol), followed by contact of the pretreated area with a nucleic acid encoding tumor antigen Pym T, showed a strong induction of a cytotoxic immune response. The office action disregards the significance of this study, pointing to the fact that the induction of CTLs was observed *in vitro* and alleging that the study does not demonstrate that the amount of activation achieved is therapeutically relevant. But the office action provides no cogitative, scientific basis for discounting the significance of these test results. Indeed, CTL assays are the currently acceptable experimental technique for determining the efficacy of a given vaccine.

Next, claims 1-24, 27 and 28 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants aver that the amendments to the claims above obviate this rejection as it applies to claims 1-19. With respect to claims 27 and 28, Applicants are unclear how to respond to this rejection, as there is no basis for rejection of these claims provided in the office action. For purposes of this response, Applicants assume that the inclusion of claims 27 and 28 under this rejection was inadvertent. With respect to claims 20-24, Applicants assert that the term "extended" is not unclear, and that it simply refers to the increase in time that transgene expression occurs that is attributable to treatment or pretreatment with a mucous membrane disruptive agent. Reconsideration and withdrawal of this §112, second paragraph, rejection is requested.

Finally, claims 20-25 and claim 26 are rejected under 35 U.S.C. §102(b) as anticipated by Henning *et al.* and Woo *et al.*, respectively. Applicants assert that the amendments to claims 20 and 26 overcome this rejection. Claim 20 has been amended to recite alcohol as the disruptive agent. Claims 21-25 are dependent on claim 20 and are interpreted to comprise all of the limitations in claim 20. Henning *et al.* mentions that N-

acetylcysteine, dithiothreitol, pepsin and pilocarpine are mucolytic agents that can be used with the methods taught in Henning *et al.* However, Henning *et al.* provides no suggestion that alcohol can be used as a disruptive agent. This distinction is important because Applicants found that pretreatment with a solution of ethanol (a mucodisruptive agent) caused a surprising and unexpected increase in transgene expression, which was well-above that observed with pretreatment using dithiothreitol (a mucolytic agent; see Example 7 of the subject application). Applicants are prepared to submit an expert declaration in further support of this position.

In view of the foregoing amendments and remarks, Henning *et al.* fails to anticipate claims 20-25, as it does not teach all of the elements of the claims, i.e., alcohol as a disruptive agent. Furthermore, in anticipation of a possible obviousness rejection, Applicants assert that the superior, unexpected results obtained when using alcohol is an unobvious discovery nowhere taught or suggested in Henning *et al.* Accordingly, Applicants respectfully request the reconsideration and withdrawal of this §102(b) rejection as it applies to claims 20-25.

With respect to the rejection of claim 26, the office action cites Woo *et al.* as teaching a suppository comprising a nucleic acid vector encoding a gene. Applicants assert that the amendment to claim 26 above obviates this rejection. Claim 26 has been amended to recite that the suppository induces an immune response in a recipient thereof. The teachings of the Woo *et al.* are limited to the use of vectors for gene therapy; nowhere does Woo *et al.* teach or suggest that its suppository is used as a vaccine or to modulate or induce an immune response. Since Woo *et al.* does not teach all of the limitations of claim 26, it fails as an anticipatory reference. Reconsideration and withdrawal of this §102(b) rejection of claim 26 is requested.

Applicants assert that all pending claims are in condition for allowance, and such action is respectfully requested. The Examiner is invited to call the undersigned if clarification is needed on any aspect of this Amendment, or if the Examiner believes a telephonic interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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